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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/774,802	02/09/2004	Kari Alitalo	28967/34891.1	9059
4743	7590	11/20/2006		
MARSHALL, GERSTEIN & BORUN LLP 233 S. WACKER DRIVE, SUITE 6300 SEARS TOWER CHICAGO, IL 60606			EXAMINER DANG, IAN D	
			ART UNIT 1647	PAPER NUMBER

DATE MAILED: 11/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

10/774,802

Applicant(s)

ALITALO, KARI

Examiner

Ian Dang

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 23 October 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 43-93 is/are pending in the application.
- 4a) Of the above claim(s) 43-80 and 85-93 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 81-84 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |                                                                                                                       |                                                                                         |
|-----------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                           | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____                                                |

## **DETAILED ACTION**

### ***Election/Restrictions***

Applicant's election with traverse of Group X, claims 81-84 in the communication filed on 10/23/2006 is acknowledged. Applicant has further elected sub-invention D, which is directed to a soluble polypeptide comprising a fragment of Flt4, wherein the polypeptide and fragment are capable of binding to a human VEGF-C. The traversal is on the ground that Group X is related to all the other groups and there is no undue burden to search the other groups. This is not found persuasive for the following reasons:

Applicant's attention is directed to MPEP 808.02 which states that "Where the related inventions as claimed are shown to be distinct under the criteria of MPEP 806.05(c-I), the examiner, in order to establish reasons for insisting upon restriction, must show by appropriate explanation one of the following: (A) Separate classification thereof; (B) A separate status in the art when they are classifiable together; (C) A different field of search." As set forth in the Restriction requirement, the separate classification established for each Group demonstrates that each distinct Group has attained recognition in the art as a separate subject for inventive effort, and also a separate field of search. Thus, the Restriction requirement is proper.

Applicant argues that no burden is placed on the examiner to consider all claims. As discussed above, the separate classification established for each Group demonstrates that each distinct Group requires a separate field of search, and a search of one Group would not reveal art on the other Groups, thus imposing a burden on the examiner. Furthermore, each group requires a non-coextensive sequence and non-patent literature search.

The requirement is still deemed proper and is therefore made FINAL. Claims 43-80 and 85-93 are withdrawn from further consideration pursuant to 37 CFR 1.142(b).

Claims 81-84 are pending and under examination.

### ***Specification***

When there are benefit claims to multiple prior nonprovisional applications (e.g., a string of prior nonprovisional applications), the relationship must include identification of each nonprovisional application as either a continuation, divisional, or continuation-in-part application of a specific prior nonprovisional application for which a benefit is claimed. See United States Patent and Trademark Office OG Notices: 1268 OG 89 (18 March 2003).

Further, the specification on page 1, paragraph 1, should be amended to reflect the status of priority applications USSN 09/929,612 (now US Patent No. 6,706,870), USSN 08/250,846 (now US Patent No. 6,562,333), USSN 08/177,747 (abandoned), and USSN 08/077,203 (abandoned).

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 81-84 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting lymphangiogenesis in a mammalian organism having a disease characterized by expression of Flt4 tyrosine kinase in blood vessels, does not reasonably provide enablement for a method of inhibiting genesis of blood vessels in a mammalian organism having a disease characterized by expression of Flt4 tyrosine kinase (Flt4) in blood vessels. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

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In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include: (1) Nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the breadth of the claims, (7) the quantity of experimentation needed, (8) relative skill of those in the art.

#### Nature of the invention and breath of the claims

The claims are drawn to a method of inhibiting genesis of blood vessels in a mammalian organism having a disease characterized by expression of Flt4 tyrosine kinase (Flt4) in blood vessels. The invention is broad because the recitation of claims 81-84 encompasses the formation of old and new blood vessels from existing vessels by angiogenesis and new blood vessels by vasculogenesis. These 2 types of biological processes have distinct signals and are induced under different conditions.

#### Unpredictability and state of the art

The state of the art for the role of Flt4 in the formation of the lymphatic vasculature is well established. Alitalo et al. (2005) teach the mechanisms for lymphangiogenesis in development and human disease in a recent review article.

However, the role of Flt4 in the formation of blood vessel is not predictable. Tammela et al. (2005) teach that Flt4 or VEGFR-3 is present in all endothelial during development but in the adult it becomes restricted to lymphatic endothelial cells and certain fenestrated blood vascular endothelial cells. VEGFR-3 is upregulated on blood vascular endothelial cells in pathologic conditions, such as vascular tumors and in the periphery of solid tumors (page 556, column 1,

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1<sup>st</sup> paragraph). While the role of Flt4 on existing endothelial is well studied, the art is silent in the role of Flt4 in the genesis of blood vessels.

In addition, the VEGF-C, the ligand for Flt4, is not involved with the formation of new blood vessels from existing blood vessels. Ferrara et al. (1999) teach that a K14-driven VEGF-C transgene induced lymphangiogenesis but no angiogenesis in mouse skin, and recombinant VEGF-C also stimulated lymphatic vessel hyperplasia in mature chick chorioallantoic membrane (page 1362, column 2, 2<sup>nd</sup> paragraph).

In view of these teachings, a method of inhibiting genesis of blood vessels in a mammalian organism having a disease characterized by expression of Flt4 tyrosine kinase (Flt4) in blood vessels is not predictable.

#### The amount of direction or guidance present

Applicants' disclosure is limited to the identification of genes responsible for affecting sleep in flies. The specification does not provide guidance or direction regarding how can Flt4 be involved in the formation of blood vessels and how the inhibition for the genesis of blood vessels can be mediated through Flt4. Since Applicants have not linked the expression of Flt4 with the formation of blood vessels, Flt4 may not have any effects on the formation of blood vessels.

#### Working Examples

Although Applicants have provided several examples for a method of inhibiting the formation of lymphatic system, the specification does not provide any examples for a method of inhibiting genesis of blood vessels in a mammalian organism having a disease characterized by expression of Flt4 tyrosine kinase (Flt4) in blood vessels. Flt4 is a critical protein for lymphangiogenesis, but its role for the formation of blood vessels in angiogenesis or

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vasculogenesis has not been illustrated in any examples in the specification of the instant application.

The quantity of experimentation needed

Because the claims are broadly drawn to a method of inhibiting genesis of blood vessels in a mammalian organism having a disease characterized by expression of Flt4 tyrosine kinase (Flt4) in blood vessels, and because Applicant's disclosure does not contain sufficient teachings to overcome the unpredictability taught in the art, it would require undue experimentation by one of skill in the art to be able to practice the invention commensurate in scope with the claims.

**Conclusion**

No claims are allowed.

**Information**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ian Dang whose telephone number is (571) 272-5014. The examiner can normally be reached on Monday-Friday from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ian Dang  
Patent Examiner  
Art Unit 1647  
November 8, 2006

  
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